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National Advisory Committee on Immunization (NACI)*

SUPPLEMENTARY STATEMENT ON MEASLES ELIMINATION IN CANADA

Summary

Elimination of indigenous measles by the year 2000 is a highly desirable goal, shared by all countries of the Americas. To achieve it in Canada, a two-dose immunization schedule must be implemented and completed by all children within the next few years. This is best achieved by beginning the routine administration of a second dose of vaccine to a specified cohort of young children and by implementing short-term "catch-up" programs to revaccinate all children over the recommended age for the second dose. Considerable latitude is possible in the design of catch-up programs but common initiation periods among provinces and territories would aid public education activities, facilitate immunization programs and reduce costs through large volume vaccine purchases.

Introduction

Measles is a severe respiratory tract infection frequently complicated by pneumonia, croup, sinusitis, otitis media and febrile convulsions[1]. Nearly one million measles deaths still occur annually in children worldwide[2]. Measles is the most contagious infection of humans, able to spread even when only a small proportion of case contacts are susceptible[3]. The available live, attenuated measles vaccines are safe and effective[4]. Among children vaccinated after the first birthday, about 90% to 95% develop protective immunity.

Experiences of the past decade indicate that outbreaks of measles can occur in populations with virtually 100% vaccination rates[3,5], resulting from spread of virus among the small proportion of children who failed to respond to primary vaccination or, less commonly, who lost protection over time after vaccination. The typical pattern of measles in highly vaccinated populations is one of outbreaks at extended intervals, involving 1% to 5% of school children, with spillover into pre-school children. Control measures, such as exclusion from school and mass revaccination, are disruptive, expensive and of limited effectiveness[6]. The occurrence of outbreaks inevitably causes members of the general public to question the efficacy of measles vaccine.

The administration of a second dose of measles-containing vaccine has been shown to diminish substantially the proportion of susceptible children[7,8], decreasing the potential for outbreaks from imported cases. Countries that have successfully delivered two-dose programs have virtually eliminated indigenous measles[9]. As more countries reach this goal, it becomes possible to envision global eradication of measles, as was achieved with smallpox and is near with poliomyelitis. A major dividend from aggressive efforts to eradicate measles globally will be the opportunity to discontinue measles vaccination programs altogether, sparing future generations from these costs.

In December, 1992, following large outbreaks of measles in several provinces, a National Consensus Conference on Measles was held in Ottawa[10]. Participants endorsed the goal to eliminate indigenous measles in Canada by the year 2005. It was recognized that this would require near universal uptake of the initial dose of vaccine, as well as new programs to deliver a second dose before school entry. NACI subsequently advocated a routine two-dose measles vaccination schedule[11].

In September, 1994, the Federal Health Minister, the Honourable Diane Marleau, resolved (Resolution CSP24R16) with representatives of other nations at the XXIV Pan American Sanitary Conference to eliminate measles from the Americas by the year 2000. To date, competing developments in childhood vaccination programs have pre-empted the formal introduction of

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two-dose measles programs in Canada. In provinces with physician-based vaccine delivery, some second doses are being given on an ad hoc basis, but such an approach lacks the benefits of an organized program.

A "laissez-faire" approach was acceptable in 1993 when Canada enjoyed the lowest level of measles activity ever recorded. Only 204 suspected cases were reported (0.7/100,000 population). Three provinces and the territories reported no cases and four additional provinces reported fewer than 12 cases each. The lull ended in 1994 when reports jumped to 523, a 2.5-fold increase. An additional sharp increase has been evident in 1995, driven in part by renewed outbreaks in Ontario. The provisional total to 31 October, 1995, exceeded 2,100 cases. This total is about 10-fold greater than for the United States during the same period and represents over 50% of cases reported in the Western Hemisphere in 1995. Other countries in the Americas have recently conducted highly effective mass measles vaccination campaigns or have already implemented routine two-dose programs[9] and are experiencing few cases in spite of heightened surveillance activities. Consequently, the approach taken in Canada to date is overtly the least effective. Sufficient numbers of unprotected children exist in every province to give rise to outbreaks at any time. Mathematical modelling of the Canadian situation predicts that outbreaks involving upwards of 20,000 true cases nationwide are possible.

Recommendations

1. All provinces and territories should make a commitment to eliminate indigenous measles, as recommended by the Measles Consensus Conference and by NACI.

   To do so by the year 2000 would place Canada in step with other members of the Pan American Health Organization (PAHO).

2. A first dose of measles-mumps-rubella (MMR) vaccine should continue to be given to all eligible children, as soon as practicable after their first birthday.

3. A second dose of MMR vaccine should be offered routinely at least 1 month after the first dose, to raise protection rates as high as possible.

   It would be most convenient to link this dose with other routinely scheduled vaccinations. Options include giving it with the next scheduled vaccinations at 18 months of age, or with school-entry vaccinations at 4 to 6 years of age, or at any intervening age that is practicable (such as at entry to day care). Provinces should determine a preferred time for administration of second MMR doses.

4. For the earliest elimination of measles, a second dose of measles vaccine should be provided, as part of special catch-up programs, to all children and adolescents previously immunized under the one-dose schedule.

   Without a catch-up program, giving a second dose only to young children may not eliminate outbreaks for 10 to 15 years, or until after the year 2005, which is inconsistent with the PAHO target.

   Numerous models exist for carrying out catch-up programs[9]. Many PAHO countries have successfully used mass vaccination campaigns lasting 1 to 7 days. The United Kingdom recently achieved 94% uptake among school children over a 4-week period. Other acceptable options would include programs extending over several months or even a few years. In the latter approach, several grade cohorts are vaccinated annually until all children have been included. With extended programs, efforts may be confounded by the occurrence of outbreaks in children not yet revaccinated. However, the success of similar programs in other countries will likely reduce the frequency of imported cases that ignite outbreaks.

   Nevertheless, the faster catch-up programs are completed, the greater their impact will be in preventing major outbreaks.

5. The necessary infrastructure should be included in the design of two-dose programs to maximize their effectiveness.

   Necessary supportive measures include intensive surveillance and rapid reporting of all suspected measles cases; availability of reliable tests to confirm the diagnosis of measles; achievement and maintenance of documented proof of immunization in the entire population at risk; and prompt outbreak control measures designed to prevent spread to susceptible contacts until all susceptibles have received a second dose.

Vaccine Considerations

For routine second doses, MMR vaccine is preferred because a proportion of children will also derive protection against rubella and mumps. In serosurveys carried out at various intervals following routinely administered first doses of MMR vaccine, about 1% to 6% of children vaccinated after the first birthday lacked antibody to rubella[12,13,14] and 3% to 19% lacked antibody to mumps[12,14,15], in addition to the 2% to 12% lacking antibody to measles[12,15,16]. Component-specific failures to respond seldom co-exist in individual children. Most non-responders make and retain protective antibody responses upon revaccination[17], regardless of the antigen in question. Measles vaccination remains highly cost effective even with the addition of a second MMR dose (unpublished observations).

Use of monovalent measles vaccine is acceptable for special catch-up programs, although some benefits would be derived by including rubella and mumps vaccines. Because special catch-up programs involve large target populations, the choice of vaccine is influenced by cost considerations, the limited range of licensed combination vaccines and the age of the population targeted. In Canada, only monovalent measles vaccine and MMR vaccine are currently licensed, although a measles-rubella (MR) vaccine could shortly become available. Monovalent measles vaccine is substantially cheaper than MMR vaccine.

MMR or measles vaccine can be given concurrently with other routinely used childhood vaccines[18], such as diphtheria toxoid, pertussis vaccine and tetanus toxoid (DPT)-based combination vaccines. Separate injections are required, in opposite limbs. The minor adverse effects of co-administered MMR and DPT-based combination vaccines are not additive because they occur at different intervals following administration. Co-administration of MMR and DPT-based combination vaccines does not overtax the child's ability to mount a normal immunologic response to each component.

Special Considerations for Catch-Up Programs

The principal target group for a catch-up campaign is school children because they had the highest rates of measles in recent Canadian outbreaks and are most readily identified and served. Ideally, all children in grade schools would be included. The upper and lower age limits should be set taking into consideration local disease epidemiology. All age groups through early adulthood contain persons at risk of measles but too few outbreaks in Canada have involved college and university students to recommend their routine inclusion in such programs.

Children who have already received two doses of a measles-containing vaccine at appropriate ages can be exempted if documentation is readily available. When immunization records are incomplete or unavailable, there is no concern about proceeding with immunization because no harm is done by administering measles vaccine to immune individuals.

Catch-up campaigns require extensive education of health professionals and the general public. Promotional activities would be most efficient if uniformity existed among the programs offered by the provinces and territories. Coordination of starting dates may be more crucial than similarity of other program parameters, such as scope and duration. An additional advantage of coordinated programs is the opportunity to reduce vaccine costs through combined large volume purchases.

Adverse Effects of Second Doses of Measles Vaccine

The adverse effects of a primary dose of measles vaccine are described in the *Canada Immunization Guide*[11]. Only 5% to 15% of persons receiving a second dose will experience a "primary take", with the potential to cause the same minor adverse effects seen after primary doses. Older children appear to have less risk of high fever 7 to 10 days following measles vaccination than infants. Older children may complain of transient stinging at the injection site. School-wide vaccination campaigns are unlikely to result in illness symptoms that would increase absenteeism or disrupt academic or athletic programs.

The risk of rubella vaccine-associated arthralgia or acute arthritis, although present, is very low in the age group 5 to 19 years. Acute arthritis is rarely seen in persons vaccinated prior to 16 years of age and affects only occasional vaccinees aged 17 to 25 years, after which it becomes more frequent, particularly in women. Only 1% to 6% of revaccinated children will experience vaccine-induced primary infection with the attendant possibility of adverse effects.

Precautions and Contraindications to a Second Dose of Measles Vaccine

Administration of live, attenuated measles vaccine is contraindicated in persons of any age whose immune system is impaired by disease or medication.

Measles vaccination is, nevertheless, indicated for most infants infected with the human immunodeficiency virus (HIV), whose immune function at 12 to 15 months of age is compatible with safe MMR vaccination[19]. Second doses of measles vaccine should also be safe later in the second year of life and are recommended. The safety of doses at later ages is uncertain because immune function can be expected to decline with age.

Children who had a true anaphylactic reaction to their first dose of MMR vaccine should not be revaccinated. Persons with anaphylactic hypersensitivity to hen's eggs may rarely react to the small quantity of ovalbumen-like protein in measles vaccine[20]. Allergy to eggs is often outgrown and is rarely reported as a life-threatening condition among school-aged children. Children who safely received a first dose of MMR vaccine in spite of having evidence of being allergic to eggs at the time should be at minimal risk of anaphylaxis with a second dose. Similarly, "egg-allergic" children who tolerate small quantities of egg in foods are at minimal risk of anaphylaxis with vaccination. Therefore, skin testing for MMR allergy is not required for second doses of the vaccine. Whenever vaccines are administered, it is prudent to ensure that all children are supervised for at least 15 minutes afterward and that treatment can be instituted promptly if signs of anaphylaxis develop[21,22].

Fever $\geq 39.4^{\circ}$ C occurs in 5% to 15% of young children following measles vaccination and a small proportion of these children have febrile seizures. Fever as a result of vaccination is restricted to susceptible subjects so the risk of seizures with a second dose of measles vaccine is very low. The risk is further reduced when the second dose is given to children of school age because susceptibility to simple febrile convulsions subsides after 5 years of age.

Immunization should not be delayed because of minor illness, with or without mild fever. This is particularly relevant for school-based campaigns, when a proportion of children will inevitably have cough or cold symptoms. The response to vaccination is not impaired in subjects with concurrent mild infections[23,24].

A consideration in targeting adolescents and young adults for vaccination with live virus vaccines is the possibility of pregnancy, a contraindication to vaccination. Pregnant persons should be given the opportunity to refuse vaccination. In the event that measles vaccination is administered to someone subsequently found to be pregnant, it is reassuring to know that no clear evidence of teratogenicity exists in spite of 25 years of experience with this vaccine[25]. Active screening for pregnancy prior to administering monovalent measles vaccine in large campaigns is not essential. The teratogenic potential of RA27/3 rubella vaccine is of more concern, but studies in accidentally exposed women indicate an observed risk of fetal injury of 0% and a theoretical maximum risk of 2%[26]. Pregnancy screening protocols should be developed if MR or MMR vaccine is targeted for use in age groups likely to be sexually active.

Large-scale catch-up campaigns inevitably attract public and media attention, warranting careful explanation of benefits and risks. NACI and the Laboratory Centre for Disease Control pay close attention to reports of rare, serious adverse events following administration of vaccines. No substantiated evidence exists to support speculation that measles vaccine can cause Crohn's disease or Guillain-Barré syndrome (GBS). None of 63 cases of GBS reported in Canadian children since 1991 had been vaccinated within the previous 30 days. The Institute of Medicine in the United States[27] concluded that evidence was inadequate to accept or reject a causal relationship between measles vaccination and encephalitis, subacute sclerosing panencephalitis, optic neuritis, transverse myelitis, GBS, and diabetes mellitus.

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International Notes

BRUCELLOSIS ASSOCIATED WITH UNPASTEURIZED MILK PRODUCTS ABROAD — UNITED KINGDOM

Two cases of acute brucellosis in members of a family who stayed abroad during April 1995 were reported recently to the Public Health Laboratory Service, Communicable Disease Surveillance Centre (CDSC). They developed minor non-specific symptoms and intermittent fever in early June and were admitted to hospital in England in late July. *Brucella melitensis* was cultured from the blood of one case; serologic tests were weakly positive for the other. They both had eaten a locally produced cheese pastry during their stay abroad.

A total of nine human cases of brucellosis in England and Wales in 1995 have been reported to CDSC. *B. melitensis* was isolated from five cases and the other four were identified serologically. Six cases, all of whom had consumed goats' milk and/or cheese, were known to be associated with travel.

CDSC received 44 laboratory reports of human brucellosis infections from 1992 to 1994 (16 in 1992, 7 in 1993, 21 in 1994). Nine of these were due to *B. melitensis* and the others were associated with *B. abortus* or *Brucella* sp. Twenty-two cases were reported to have been acquired abroad.

Brucellosis due to *B. melitensis* has never been reported in animals in Great Britain. An outbreak of brucellosis caused by *B. abortus* occurred in 1993, due to imported infected cattle. This was eliminated by slaughter of infected cattle and tracing of contacts.

There are very few reports of indigenously acquired human cases of brucellosis in Great Britain because almost all milk is pasteurized and the program to eradicate bovine brucellosis has been successful. Most cases are chronic infections acquired at work. Acute imported human infections continue to be reported, often associated with the consumption of raw milk or cheese. Brucellosis may not be considered early in the course of the disease and diagnosis may therefore be delayed.

Source: *WHO Weekly Epidemiological Record, Vol 70, No 43, 1995.*

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